

## **REMARKS/ARGUMENTS**

The foregoing amendments in the specification and claims are of formal nature, and do not add new matter.

The paragraph beginning at page 1, immediately following the title, has been replaced. The "replacement paragraph" submitted herein was first added to the specification by a preliminary amendment filed on August 21, 2002. However, the filing receipt mailed September 12, 2003, did not reflect the amended priority. Consequently, a Request for Corrected Filing Receipt, attaching the preliminary amendment of August 21, 2002, was filed on October 21, 2003. In response, a corrected filing receipt reflecting the correct priority, as disclosed in the "replacement paragraph" submitted herein, was mailed by the PTO on October 31, 2003. Applicants kindly request that the Examiner verify that the "replacement paragraph" as submitted in the preliminary amendment of August 21, 2002, has been made of record in the application. If it has not been made of record, then the Examiner is kindly requested to make it of record in the application by entering it immediately following the title of the application, in lieu of any other priority-claiming paragraphs.

Further, Applicants submit that the "replacement paragraph" submitted herein (which is the same as that submitted in the preliminary amendment of August 21, 2002), includes the relationship to parent applications as well as the status of non-provisional parent applications.

Prior to the present amendment, claims 58-77 were pending in this application. With this amendment, claims 66, 67 and 71-73 have been cancelled without prejudice, and claims 58-63 have been amended to clarify what applicants have always regarded as their invention. Claims 58-65, 68-70 and 74-77 are pending after entry of the instant amendment. Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

### **I. Priority**

The PTO states that if Applicants desire priority under 35 U.S.C. §§ 119(e), 120, 121 or 365(c) based upon a previously filed application, specific reference to the earlier-filed application must be made in the instant application. Applicants respectfully submit that priority

to earlier-filed applications was claimed at the time the instant application was filed (*i.e.*, on October 24, 2001). The priority to earlier-filed applications was amended by preliminary amendment on August 21, 2002. Applicants respectfully submit that the priority claimed in the preliminary amendment of August 21, 2002, or, in the alternative, that submitted herewith, is proper and meets the PTO's requirements that the relationship to parent applications as well as the status of non-provisional parent applications be included.

## **II. Specification**

(A) As requested by the PTO, the ATCC address on page 376, line 34, has been amended. Applicants submit that Applicants recently made a photocopy of U.S. Application 09/918,585 filed 7/30/2001, of which the instant application is a continuation, from the PTO's files. According to this photocopy of the application as filed, the paragraph containing the ATCC address begins on page 376, line 34; not on page 372, as cited in the instant Office Action.

Further, Applicants respectfully submit that all references to page and line numbers made throughout this response will be based on the application photocopied from the PTO files by the Applicants.

(B) The embedded hyperlink cited by the PTO as well as other embedded hyperlinks and/or browser-executable code have been deleted.

In view of the above, Applicants respectfully request that the objections to the disclosure be withdrawn.

## **III. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

(A) Claims 58-77 are rejected under 35 U.S.C. §112, second paragraph, for allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The PTO notes that "PRO337 is a soluble protein and is not disclosed as being expressed on a cell surface. Accordingly, the PTO states that the recitation that the claimed nucleic acid encodes a protein that comprises an "extracellular domain" and the recitation of "the extracellular domain ... lacking its associated signal sequence" is indefinite.

Without acquiescing to any of the rejections, Applicants submit that the cancellation of claims 66, 67 and 71-73 renders the rejection of these claims moot. Further, none of remaining claims 58-65, 68-70 or 74-77 recites a nucleic acid encoding an extracellular domain of a polypeptide or an extracellular domain of a polypeptide lacking its associated signal peptide. Accordingly, Applicants request that the rejection of claims 58-65, 68-70 and 74-77 under 35 U.S.C. §112, second paragraph, be withdrawn.

**(B)** Claims 71-73 are further rejected under 35 U.S.C. § 112, second paragraph, because the exact meaning of the term “hybridizes” or the phrase “hybridization occurs under stringent conditions” is not clear.

Without acquiescing to these rejections, Applicants submit that the cancellation of claims 71-73 renders the rejection of these claims moot. Accordingly, Applicants request that the rejection of claims 71-73 under 35 U.S.C. §112, second paragraph, be withdrawn.

#### **IV. Claim Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)**

Claims 58-62 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. In particular, the PTO notes that “[t]he claims are drawn to polynucleotides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence . . . [without requiring] that the polypeptide encoded by the polynucleotide possess any particular biological activity . . . .”

Without acquiescing to the rejection, Applicants respectfully submit that amended claims 58-62 now recite the functional limitation that the polypeptide is a mitogen for inner ear supporting cells. Accordingly, the PTO’s allegation that the claims are drawn to a genus of polynucleotides defined by sequence identity alone is no longer true. Coupled with the general knowledge available in the art at the time of the invention, the specification provides ample written support for polypeptides encoded by such polynucleotides. For example, Example 116 (page 351) of the specification describes assays for determining the ability of polypeptides to act as mitogens for inner ear supporting cells. As described therein, such cells are auditory hair cell progenitors and, therefore, the mitogenic polypeptides are useful for inducing the regeneration of

auditory hair cells and treating hearing loss in mammals. Thus based on the high percentage of sequence identity and the described assay for the mitogenic property, one skilled in the art would have known at the time of the invention, that Applicants had possession of the claimed polynucleotides.

The PTO is therefore respectfully requested to reconsider and withdraw the rejection of claims 58-62 for allegedly lacking written support.

**V. Claim Rejections Under 35 USC § 112, First Paragraph (Enablement)**

A. Claims 58-62 and 70-77 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Specifically, the PTO alleges that “[t]he specification lacks complete deposit information for the deposit of the cell line containing cDNA deposited under ATCC accession No. 209487 [and that it] is not clear that the cDNA deposited as ATCC accession no. 209487 is known and publicly available or can be reasonably isolated from nature without undue experimentation or is the same as SEQ ID NO:522 . . . .”

The PTO further alleges that Applicants’ referral to the deposit of the cDNA on page 372 (page 376 of the photocopied application) “is an insufficient assurance that the required deposit has been made and all the conditions of 37 C.F.R. §§ 1.801-1.809 met.”

Without acquiescing to any of the rejections, Applicants submit that the cancellation of claims 71-73 renders the rejection of these claims moot.

Regarding the rejection of claims 58-62, 70 and 74-77, Applicants submit that the specification has been amended on page 376 to provide complete deposit information for the deposit of the cell line containing cDNA deposited under ATCC Accession No. 209487. In addition the amended paragraph on page 378 makes it clear that the deposited cDNA is publicly available and that any restrictions will be irrevocably removed upon grant of a patent. The PTO’s doubts as to whether the cDNA “can be reasonably isolated from nature without undue experimentation” is without merit. Example 96, on page 315 of the specification describes, in detail, the method of isolating cDNA that encodes PRO337. Further, the cDNA has been deposited with ATCC and is publicly available.

Further, Applicants respectfully submit that the disclosure on page 315, lines 10-14, makes it adequately clear that the deposited cDNA is the same as SEQ ID NO:522. Lines 10-11 of page 315 disclose that “[t]he full length nucleotide sequence of [clone] DNA43316-1237 is shown in Figure 221 (SEQ ID NO:522),” and lines 13-14 disclose that “[c]lone DNA43316-1237 has been deposited with ATCC and is assigned ATCC deposit no. 209487.”

Applicants therefore submit that the specification does not lack deposit information for the deposit of the cell line containing cDNA deposited under ATCC accession No. 209487 and that it is clear that the cDNA deposited as ATCC accession no. 209487 is publicly available and that it is the same as SEQ ID NO:522.

Lastly, in response to the PTO’s allegations that Applicants’ referral to the deposit of the cDNA is an insufficient assurance that the required deposit has been made and all the conditions of 37 C.F.R. §§ 1.801-1.809 met, Applicants respectfully submit that, as stated in the specification at, for example, page 378, the deposit has been made under the provisions of the Budapest Treaty. In compliance with the requirements necessary when deposits are made under the provisions of the Budapest Treaty, the paragraph beginning on page 378, line 33, has been amended to include language that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent on this application.

Applicants believe that the language of the amended paragraph beginning on page 378, line 33, should suffice as assurance that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. Accordingly, Applicants respectfully submit that the required conditions of 37 C.F.R. §§ 1.801-1.809 are met and that no affidavit or declaration is necessary.

In view of the above, the PTO is respectfully requested to reconsider and withdraw the rejection of claims 58-62 and 74-77 under 35 U.S.C. §112, first paragraph.

**B.** The PTO further alleges that claims 58-62 and 71-77 stand rejected under 35 U.S.C. §112, first paragraph, because the specification, “while being enabling for DNA encoding SEQ ID NO:523, DNA of SEQ ID NO:522 and DNA of ATCC no. 209487” allegedly does not

reasonably provide enablement for DNAs that are 80%, 85%, 90%, 95% or 99% identical to the DNA of SEQ ID NO:522 and do not encode the polypeptide of SEQ ID NO:523. Specifically, the PTO asserts that “[t]here is no functional limitation in the claims as far (sic) as to the polynucleotide that encodes the polypeptide.”

Without acquiescing to any of the rejections, Applicants submit that the cancellation of claims 71-73 renders the rejection of these claims moot. Further, Applicants submit that remaining claims 58-62 and 74-77 recite a functional limitation for the nucleic acid, namely, that the nucleic acid encodes a polypeptide that is a mitogen for inner ear supporting cells.

In addition, Applicants respectfully submit that the PTO has erred in determining that the utility for polypeptides encoded by nucleic acids of the invention is based on the homology of the polypeptide to human neurotrimin, and further, in determining that the specification does not teach an activity for the polypeptides.

As disclosed in Example 116 (page 351) of the specification, the polypeptides encoded by nucleic acids of the invention act as mitogens for inner ear supporting cells that are auditory hair cell progenitors. These polypeptides are therefore useful for inducing the regeneration of auditory hair cells and thereby treating hearing loss in mammals. Example 116 further teaches how a polypeptide can be assayed for its ability to act as a mitogen for inner ear supporting cells. Applicants therefore submit that they have demonstrated that the specification discloses a substantial, specific and credible utility for the polypeptides encoded by the nucleic acid molecules of the invention. Further, this use is now recited in claims 58-62 and 74-77. Coupled with the general knowledge available in the art at the time of the invention, the high percentage of sequence identity and the described method to assay for the mitogenic property of the polypeptides, it would not require undue experimentation for one of skill in the art to apply the teachings of the present disclosure so as to practice the claimed invention. Accordingly, Applicants request the PTO to reconsider and withdraw the rejection of claims 58-62 and 74-77 under 35 U.S.C. §112, first paragraph.

**VI. Claim Rejections Under 35 U.S.C. § 102(b)**

Claims 71-73 are rejected under 35 U.S.C. § 102(b) as being anticipated by Struyk *et al.* Further, claims 71-72 are rejected under 35 U.S.C. § 102(b) as being anticipated by page 557 of the 1991 Boehringer Mannheim Catalog.

Without acquiescing to either of these rejections, Applicants submit that the cancellation of claims 71-73 renders the rejection of these claims moot. Accordingly, Applicants request that the rejection of claims 71-73 under 35 U.S.C. §102(b) as being anticipated by Struyk *et al.* and the rejection of claims 71-72 under 35 U.S.C. §102(b) as being anticipated by page 557 of the 1991 Boehringer Mannheim Catalog be withdrawn.


**CONCLUSION**

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (referencing Attorney's Docket No. 39780-630 P1C66).

Respectfully submitted,

Date: March 11, 2004

  
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